

STRUCTURE SEARCH

=> d his l43

(FILE 'HCAPLUS' ENTERED AT 17:23:57 ON 15 OCT 2007)

SAV L42 SHI490HCP/A

L43

4 S L42 NOT L39

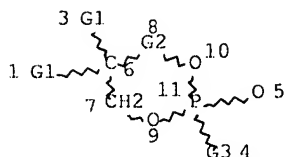
=> d que l43

L2

36 SEA FILE=REGISTRY ABB=ON PLU=ON (100-39-0/BI OR
 100-51-6/BI OR 107-88-0/BI OR 108-01-0/BI OR 124613-28-
 1/BI OR 126-11-4/BI OR 13507-10-3/BI OR 142-62-1/BI OR
 14690-00-7/BI OR 16727-61-0/BI OR 187976-16-5/BI OR
 2163-42-0/BI OR 22102-92-7/BI OR 26362-71-0/BI OR
 3443-84-3/BI OR 459-73-4/BI OR 504-63-2/BI OR 52066-54-
 3/BI OR 52692-02-1/BI OR 534-03-2/BI OR 600174-74-1/BI
 OR 600174-75-2/BI OR 600174-76-3/BI OR 600174-77-4/BI
 OR 600174-78-5/BI OR 600174-79-6/BI OR 600174-80-9/BI
 OR 600174-81-0/BI OR 600174-82-1/BI OR 600174-83-2/BI
 OR 600174-84-3/BI OR 64821-66-5/BI OR 68755-22-6/BI OR
 77-86-1/BI OR 872-99-1/BI OR 88946-00-3/BI)

L4

STR



VAR G1=H/N/O/C

REP G2=(0-1) CH2

VAR G3=N/O

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 5

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

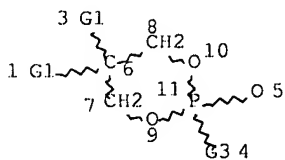
RSPEC I

NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L5 2404 SEA FILE=REGISTRY SSS FUL L4

L6 STR



VAR G1=H/N/O/C

VAR G3=N/O

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 5

DEFAULT MLEVEL IS ATOM

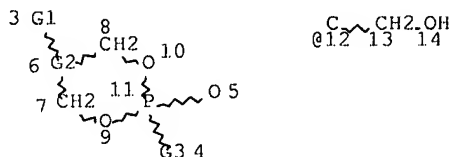
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L8 1420 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L10 STR



VAR G1=H/N/O/C
VAR G2=CH/12
VAR G3=N/O
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

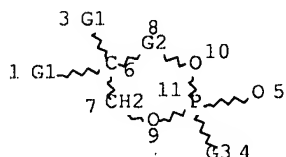
L12 539 SEA FILE=REGISTRY SUB=L8 SSS FUL L10
L13 16 SEA FILE=REGISTRY ABB=ON PLU=ON L12 AND L2
L16 54 SEA FILE=HCAPLUS ABB=ON PLU=ON L13
L17 757 SEA FILE=HCAPLUS ABB=ON PLU=ON L8
L18 399 SEA FILE=HCAPLUS ABB=ON PLU=ON L12
L19 QUE ABB=ON PLU=ON NERVE+PFT,OLD,NT/CT
L20 QUE ABB=ON PLU=ON NEURON+PFT,OLD,NT/CT
L21 QUE ABB=ON PLU=ON NERV? OR NEURON? OR AXON?
L22 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND ((L19 OR L20
OR L21))
L24 QUE ABB=ON PLU=ON L21(3A)(GROW? OR STIMUL? OR ACTIVA
T? OR PROMOT?)
L25 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND L24
L26 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 OR L22
L27 QUE ABB=ON PLU=ON PY<2003 OR PRY<2003 OR AY<2003 OR
MY<2003 OR REVIEW/DT
L28 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND L27
L31 QUE ABB=ON PLU=ON "YEDA RES?"/PA,CS,SO,CO
L32 211 SEA FILE=HCAPLUS ABB=ON PLU=ON ("SHINITSKY M"/AU OR
"SHINITSKY MEIR"/AU OR "SHINITZKY M"/AU OR "SHINITZKY
MEIR"/AU)
L33 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 AND L17
L34 25 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 AND L31
L35 29 SEA FILE=HCAPLUS ABB=ON PLU=ON L33 OR L34
L36 27 SEA FILE=HCAPLUS ABB=ON PLU=ON L35 AND L27
L37 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L36 AND ((L19 OR L20
OR L21) OR L24)
L38 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L33 AND L27
L39 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L37 OR L38
L40 8 SEA FILE=HCAPLUS ABB=ON PLU=ON ((L16 OR L17 OR L18))
AND ((L19 OR L20 OR L21))
L41 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 AND L27
L42 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L41 OR L28
L43 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L42 NOT L39

=> d his 153

(FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 17:43:02 ON 15 OCT 2007)

L53 18 S L45 NOT L52

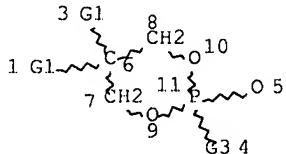
=> d que stat l53
L4 STR



VAR G1=H/N/O/C
REP G2=(0-1) CH2
VAR G3=N/O
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE
L5 2404 SEA FILE=REGISTRY SSS FUL L4
L6 STR



VAR G1=H/N/O/C
VAR G3=N/O
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE
L8 1420 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L15 5 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND (MEDLINE/LC
OR BIOSIS/LC OR DRUGU/LC OR EMBASE/LC)
L21 QUE ABB=ON PLU=ON NERV? OR NEURON? OR AXON?
L27 QUE ABB=ON PLU=ON PY<2003 OR PRY<2003 OR AY<2003 OR
MY<2003 OR REVIEW/DT
L30 QUE ABB=ON PLU=ON ("SHINITZKY M"/AU OR "SHINITZKY ME
IR"/AU OR "SHINITZKY M"/AU OR "SHINITZKY MEIR"/AU)
L31 QUE ABB=ON PLU=ON "YEDA RES?"/PA,CS,SO,CO
L44 20 SEA L15
L45 19 SEA L44 AND L27

L1 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:224038 CAPLUS

DOCUMENT NUMBER: 126:212447

TITLE: Phosphorous-containing dipeptide inhibitors of cysteine and serine protease

INVENTOR(S): Mallamo, John P.; Bihovsky, Ron; Tao, Ming; Wells, Gregory J.

PATENT ASSIGNEE(S): Cephalon, Inc., USA

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

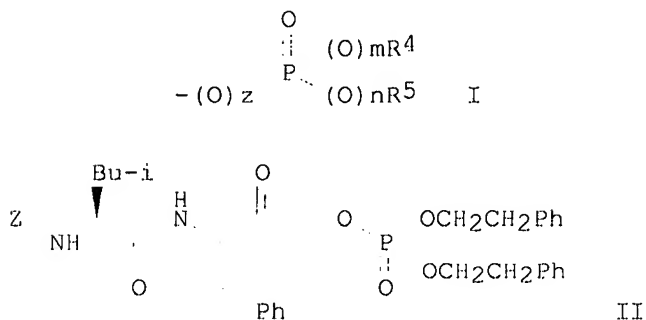
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9703679 | A1 | 19970206 | WO 1996-US11625 | 19960712 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN | | | | |
| US 5639732 | A | 19970617 | US 1996-679342 | 19960710 |
| CA 2226414 | A1 | 19970206 | CA 1996-2226414 | 19960712 |
| AU 9664583 | A | 19970218 | AU 1996-64583 | 19960712 |
| EP 871454 | A1 | 19981021 | EP 1996-923756 | 19960712 |
| EP 871454 | B1 | 20031112 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 11509231 | T | 19990817 | JP 1996-506762 | 19960712 |
| AT 253920 | T | 20031115 | AT 1996-923756 | 19960712 |
| EP 1389624 | A1 | 20040218 | EP 2003-78371 | 19960712 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| PT 871454 | T | 20040331 | PT 1996-923756 | 19960712 |
| ES 2210377 | T3 | 20040701 | ES 1996-923756 | 19960712 |
| HK 1016495 | A1 | 20040813 | HK 1999-101617 | 19990414 |
| PRIORITY APPLN. INFO.: | | | US 1995-1491P | P 19950717 |
| | | | US 1996-679342 | A 19960710 |
| | | | EP 1996-923756 | A3 19960712 |
| | | | WO 1996-US11625 | W 19960712 |

OTHER SOURCE(S): MARPAT 126:212447

GI



AB The present invention is directed to novel phosphorous-containing inhibitors of cysteine or serine proteases of the formula X-W-Y-CH(R2)-CO-NH-CH(R1)-CO-[CH(R3)]_t-Q wherein: X = e.g., C6-C14 aryl, heteroaryl with C6-C14 ring atoms, C1-C10 alkyl (un) substituted with one or more J groups, C1-C10 alkoxy; W = CO, SO₂; Y = NH, (CH₂)_k where k = 0-3; R1 and R2 are independently, e.g., H, C1-C14 alkyl (un) substituted with one or more J groups, C3-C10 cycloalkyl (un) substituted with one or more J groups; R3 = e.g., H, lower alkyl, aryl, heteroaryl; t = 0 or 1; Q = I wherein m, n, and z are independently 0 or 1; R4 and R5 are independently, e.g., H, lower alkyl (un) substituted with J, heteroaryl (un) substituted with J, or taken together to form a 5-8 membered heterocyclic ring (un) substituted with J; J = e.g., halogen, alkyl, guanidino, alkoxy. Thus, e.g., substitution reaction of Z-Leu-Phe-CH₂Br with bis(phenethyl)phosphate afforded dipeptide derivative II (Z = PhCH₂O₂C) in 62% yield which exhibited 99% inhibition of calpain I at 0.1 μM. Methods for the use of the protease inhibitors are also described.

IT 187976-16-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of phosphorous-containing dipeptide inhibitors of cysteine and serine protease)

RN 187976-16-5 CAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-(phenylmethoxy)-, 2-oxide (9CI) (CA INDEX NAME)

Ph CH₂ O

